Nova Scotia Health

CardioVascular HEALTH NOVA SCOTIA BULLETIN

IMPROVING CARDIOVASCULAR HEALTH OF NOVA SCOTIANS

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Welcome to the Cardiovascular Health Nova Scotia (CVHNS) quarterly e-mail bulletin. The Bulletin has been created to share information about the program's activities, related cardiovascular health initiatives, and ideas from around the province.

Drug Interaction Update: Proton Pump Inhibitors (PPIs) and Clopidogrel

Clopidogrel is a pro-drug requiring activation in the liver, mainly by the CYP2C19 isoenzyme. PPIs inhibit this isoenzyme which could interfere with the activation and subsequent clinical benefit of clopidogrel. PPIs have differential effects on the degree of CYP2C19 inhibition, i.e., pantoprazole does *not* inhibit CYP2C19; omeprazole is a strong inhibitor; and esomeprazole, lansoprazole and rabeprazole are moderate inhibitors.[1]

Evidence for a potential drug interaction with clopidogrel and PPIs has been accumulating.[2-9] Two early studies, presented as abstracts, came to opposite conclusions.[5,7] A sub group analysis of an RCT (CREDO) found no evidence of an interaction.[7] The second, a retrospective cohort study using the MEDCO database identified a potential drug interaction.[5] More recent follow-up of this study identified that the risk of major cardiovascular events was similar with omeprazole, esomeprazole, pantoprazole and lansoprazole (hazard ratios ranged from 1.4 to 1.6).[6] Platelet aggregation studies have reported that pantoprazole and esomeprazole do not impair the response to clopidogrel; whereas, omeprazole decreased the antiplatelet effect.[24] Authors caution that randomized studies, specifically designed to determine the impact of concomitant PPI and clopidogrel on hard *clinical* outcomes are required to determine whether these differences in platelet aggregation correlate with adverse events.

Two recent retrospective database studies, one from Canada (Juurlink et al[8]) and the other from the US (Ho et al[9]) provide additional insight into the clinical relevance of this interaction. The primary outcomes of the studies were defined differently, however both identified cases of adverse cardiac events following treatment for acute MI or ACS in patients taking clopidogrel plus a PPI compared to clopidogrel alone.

- Use of **clopidogrel plus PPI** was associated with an **increased risk of recurrent cardiac events** compared to clopidogrel without a PPI.
  - Odds ratios (adjusted) for the primary outcome were similar in both studies:
    - OR 1.27 (95% CI 1.03 to 1.57)[8]; OR 1.25 (95% CI 1.11 to 1.41)[9]
  - Odds ratios above 2 are generally indicative of real risk in case-control studies.
- The American study reported that PPI users had significantly higher rates of the secondary outcomes of rehospitalization for ACS and rates of revascularization procedures.[9]
- A sub group analysis (Juurlink) found that pantoprazole + clopidogrel was not associated with a statistically significant increase in the risk for rehospitalization (OR 1.02 95%CI 0.70-1.47). The

number of cases in the pantoprazole group was relatively small (n= 46).[8]

- In the American study, omeprazole was the most frequently used PPI; however, a small subgroup of rabeprazole users (2.9% of patients) also had increased risk for cardiac events.[9] This is of interest since rabeprazole is not thought to be a strong inhibitor of CYP2C19.
- Neither study found an increased risk in all-cause mortality.
- Additional considerations
  - Patients in the PPI groups (i.e., the cases) had greater comorbidity that could contribute to higher cardiac event rates. (e.g., diabetes, congestive heart failure, acute renal insufficiency, concomitant cardiovascular drug use).
  - Factors such as smoking status, blood pressure, family history or genetic polymorphism of CYP2C19 were not controlled for.
  - Use of ASA was not known in the Juurlink analysis since the database included primarily prescription medications.[8]
  - Whether pantoprazole should be considered differently from "other PPIs" (omeprazole, lansoprazole and rabeprazole) has been questioned. A test for between group differences suggests no statistically significant difference. [8,10]

Practice points: weigh the risks and benefits of treatment options

An on-line document published by the Canadian Association of Gastroenterology (CAG) acknowledges that current clinical evidence for these interactions is weak (observational studies) but there is a consistent signal suggesting an interaction.[11] The mechanism of interaction is biologically plausible (CYP2C19 inhibition) and there is supporting evidence from *in vitro* platelet aggregation studies. However, *definitive* conclusions cannot be made until studies are designed to address the clinical impact of the interaction and quantify differences between individual PPIs.

Until we have this evidence:

- Assess risk for GI complications and whether prophylaxis with a PPI is required.
- The CAG recommends PPI use be restricted to clopidogrel users who are at significantly increased risk of adverse GI events or who have absolute indications for a PPI, and in patients who cannot achieve satisfactory symptom control on alternative acid-reducing strategies.[10]
  - High risk of GI bleed is defined as patients with previous peptic ulcer disease or multiple co-morbidities.
  - H_2RAs such as ranitidine are not recommended for prophylaxis in high risk patients.
- Consider whether the benefits of dual antiplatelet therapy (ASA + clopidogrel) outweigh the risk of GI bleed.
- Use lowest *appropriate* dose of ASA - to reduce risk of GI bleed.
- The influence of PPI dose on this interaction has not been addressed, but standard doses (i.e., not double doses) are recommended for NSAID prophylaxis.
- It is uncertain whether one PPI has less potential for an interaction than another.
  - The limitations of current evidence (i.e., retrospective database studies, *in vitro* tests, etc.) and conflicting outcomes do not allow definitive conclusions to be drawn for the safety of one PPI over another.

- It should be noted that the primary analysis of the observational studies found an association for increased cardiovascular risk with PPIs as a group.[5,6,8,9]

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References

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Learning Opportunities

On the Other Side of the Spoon: A Dietitian's Perspective on Dysphagia & Mealtime Management, June 3, 2009, Charlottetown, PEI. Tel: 902-894-7371

Canadian Association of Neurosciences Nurses (CANN) Conference: Best Practice Nursing across the Acute Stroke Continuum Pre Conference Workshop June 9, 2009, Halifax, NS. mabon@eastlink.ca

Cape Breton Cardiology Day: 12th Annual Clinical Day in Cardiology, June 5, 2009, Membertou, NS. Contact Dr. Paul MacDonald Tel: 902-567-8007 macdonaldpaul@cbdha.ns.ca

1st Canadian Stroke Congress:
Quebec City, June 7 & 8, 2010
www.strokecongress.ca

CVHNS News

Stroke Awareness Campaign Funding
CVHNS is pleased to provide support for an upcoming stroke awareness campaign. With funding from the Department of Health, based on its ongoing commitment to improve stroke care, an extensive campaign will be developed and launched in partnership with the Heart and Stroke Foundation of Nova Scotia. The campaign, still in the early stages of planning, will build awareness among Nova Scotians regarding the signs and symptoms of stroke and will prompt action. Stay tuned for more updates on this exciting initiative.

Taking a Look at Hypertension – Jointly

On March 23rd Cardiovascular Health Nova Scotia, Diabetes Care Program of Nova Scotia and Nova Scotia Renal Program hosted a meeting to get discussions started related to potential opportunities to address hypertension in Nova Scotia. The meeting was attended by key program staff and selected staff of the Departments of Health and Health Promotion and Protection. Dr. Norm Campbell helped the group learn more about Blood Pressure Canada, the Canadian Hypertension Education Program and hypertension initiatives that have been implemented elsewhere in Canada. The day ended with small group discussions around possible initiatives for Nova Scotia and partnerships required. Stay tuned as we make decisions on our next steps.

The 2009 recommendations for hypertensive patients with diabetes are now finalized and available through Blood Pressure Canada's website (http:/hypertension.ca/bpc/).

2007 Cardiac Data Available

The provincial data for admissions to hospital for AMI and CHF has been provided to districts. We have made some adjustments to the way we report data, as well as how we determine the completion of the end of year for abstraction. This has slowed down our reporting this year, but will allow us to iron out the bugs to allow more timely reporting next year. Many thanks to the abstractors throughout the province who worked hard to get all 2007 charts abstracted!

College of Registered Nurses Telehealth Sessions

The 2008 Nova Scotia Guidelines for Acute Coronary Syndromes

Gillian Yates, Nurse Practitioner, Cardiology, CDHA

Lena MacDonald, Nurse Practitioner, Heart Health Clinic, GASHA

June 5, 2009 2-3:30 p.m.

Broadcast to: Annapolis Co Health Centre, Digby General, Eastern Shore Memorial, Hants Community Hospital, Musquodoboit Valley Memorial Hospital, QEII VG site Bethune Rm 255, Queens General, Soldier's Memorial,, St. Martha's Regional, Twin Oaks, Valley Regional Hospital

Stroke Risk Factors & Secondary Prevention

Karen Legg, Nurse Practitoner, Neurology, CDHA

Monday, June 22, 2009

Broadcast to: Aberdeen, All Saints, CB Regional, Colchester Regional, Cumberland Regional, Eastern Shore Memorial, QEII, South Shore Regional, St. Martha's Regional, Valley Regional, Yarmouth Regional

Contact: Ann Duncan, College of Registered Nurses of Nova Scotia, Continuing Nursing Education Coordinator, Tel: 902 867-4216 or ann.duncan@gasha.nshealth.ca

DHA News

Community Cardiovascular Hearts in Motion program - a collaboration between AstraZeneca Canada and GASHA

The Guysborough Antigonish Strait Health Authority (GASHA) is taking steps to deal with individuals living with or at risk

of developing cardiovascular disease in the district. A recent Canadian Community Health Survey found that residents of GASHA over 20 years of age reported the lowest physical activity rates in the province of Nova Scotia. In addition GASHA was found to have the second highest rate of diabetes in the province. On April 3rd, 2009, GASHA and AstraZeneca Canada announced a partnership to bring the Community Cardiovascular Hearts in Motion program to the district.

"As CEO of a District with a mainly rural population, this program will be of great benefit to our residents. The *GASHA Hearts in Motion* program will see patients enroll in a 12-week program of risk assessment and management, weekly exercise, nutrition and planning education. Patients will work with a collaborative team to set goals so as to decrease heart and stroke risk factors," says Kevin MacDonald, CEO of GASHA.

The Hearts in Motion program originated three years ago in Halifax's Capital Health with the assistance of a number of partners including AstraZeneca Canada. The program, which brings a traditional hospital based cardiac rehabilitation program into the community has led to measurable improvements in patients' vascular health and has now become a permanent program in Capital Health. It has now evolved and is expanding into rural Nova Scotia through the GASHA initiative.

Mark Jones, President and CEO of AstraZeneca Canada, was on hand to announce a $400,000 investment in the *GASHA Hearts in Motion* program at St. Martha's Regional Hospital.

"We are delighted to partner with GASHA and bring the *Hearts in Motion* program to the district," said Mr. Jones. "This program brings together community partners with one common goal in mind – improving the lives of residents with cardiovascular conditions and reducing the number of hospital and emergency room visits they will require in the future."

GASHA is evaluating community sites within the region and the first community to partake in the program will be announced in the near future. Contact Lena MacDonald 902-867-4720

Helpful Resources

AHA Guidelines and Scientific Statements
Valentin Fuster,
January 2009. ISBN: 978-1-4051-8463-2
Visit www.ca.wiley.com

Guidelines on Heart Failure-Update 2009
Howlett JG, McKelvie RS, Arnold JMO. et al. Canadian Cardiovascular Society Consensus conference guidelines on heart failure, update 2009: Diagnosis and management of right-sided heart failure, myocarditis, device therapy and recent important clinical trials. *Can J Cardiol 2009;* l25(2):85-105.

Canadian Perspective on ACC/AHA 2007 Focused Update
Welsh RC, Travers A, Huynh T, Cantor WJ. Canadian Cardiovascular Society Working Goup: Providing a perspective on the 2007 focused update of the American College of Cardiology and American Heart Association 2004 guidelines for the management of ST elevation myocardial infarction. *Can J Cardiol 2009;* 25(1):25-32.

Patient's Guide to Best Practice Recommendations
The Guide reflects the Canadian Best Practice Recommendations for Stroke Care and has been designed for stroke patients, their caregivers and members of the general public who want to know more about care for stroke.
Visit www.canadianstrokestrategy.ca

Innovative Ideas

Integration of the Ottawa Model for Tobacco Dependence Treatment for Hospitalized Tobacco Users, with Follow-up by Smokers' Helpline, Being Implemented in NS

Capital Health, the IWK and Cape Breton Regional Hospital are implementing the Ottawa Model for Smoking Cessation (OMSC) for hospital inpatients starting this spring as part of a Health Canada national demonstration project with the University of Ottawa Heart Institute and the Canadian Cancer Society Smokers' Helpline.

At time of admission to the unit, *The Stop Smoking Support Program* identifies inpatients that have used tobacco during the past 6 months, provides minimal intervention stop-smoking counseling and nicotine replacement therapy during hospitalization, links the patient with community resources, and provides telephone follow-up after discharge from hospital. This model led to a 15% increase in smoking cessation rates among patients six months after discharge (35%-50%).

The *Stop Smoking Support Program* will also support a systematic professional practice transformation to implement the inpatient components of the existing Capital Health, IWK Health Centre and Cape Breton Regional Hospital Tobacco Reduction Policies.

Delivery Locations: Capital Health sites – QEII Units 6.2, 8.1, 8.2, 4.1 Halifax, Dartmouth General Units 3E, 3W, 4W, Dartmouth, Hants Community Hospital Units 200 and 500, Windsor IWK Health Centre PSCU and gyne, Halifax Cape Breton Regional Hospital 4D and CCU, Sydney . For more information contact Sharon MacIntosh at Sharon.macintosh@cdha.nshealth.ca

Information on Tobacco: Getting Started

Whether you want to stop, cut down, or are simply looking for reliable information about tobacco use, Capital Health offers free programs to help you.

The programs are run by trained professionals from Capital Health's Addiction Prevention and Treatment Services and are available free to anyone living within the Capital Health District. (The district extends from Windsor to Sheet Harbour and includes the Halifax Regional Municipality.)

The programs include the following:

- An opportunity to receive support from others who are experiencing the same thing you are.
- Free smoking aids including Champix (only available in select groups)
- A positive personal message rather than a moral message to support our decision to not use tobacco.

All Capital Health tobacco intervention programs are free of charge. If you would like to take advantage of the programs, or want more information, please call 424-2025 or email krystle.sutton@cdha.nshealth.ca.

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